Viewpoint

A Thirty-Year Journey to the Creation of the First Enantiomerically Enriched Molecular Sieve

Mark E Davis

ACS Catal., **Just Accepted Manuscript** • Publication Date (Web): 18 Sep 2018

A Thirty-Year Journey to the Creation of the First Enantiomerically Enriched Molecular Sieve

By

Mark E. Davis
Chemical Engineering
California Institute of Technology
Pasadena, CA 91125
mdavis@cheme.caltech.edu

Keywords: zeolite, chiral, synthesis, catalysis, history

In 1987, our research on how to synthesize a chiral zeolite began. Finally, in 2017, my co-workers and I succeeded in preparing and characterizing the first enantiomerically enriched molecular sieve. Here, I recount how we initiated our work on synthesizing a chiral molecular sieve, the lessons learned from the many failures we had over the years, and what were some of the key advances that ultimately led to the successful synthesis and proof that we had in fact prepared an enantiomerically enriched molecular sieve. I have no doubts that numerous other chiral molecular sieves will now be elucidated, and that clever applications of these materials will ultimately be realized.

Introduction

The synthesis of a chiral molecular sieve has been a long-standing goal in the field of zeolites and molecular sieves (as I reported years ago[1-3]), because this type of inorganic material could open new avenues for asymmetric catalysis and chiral separations. The robust nature of these porous solids could show commercial advantages in chiral processes, as these materials are easily regenerated and thus used for many cycles of performance. That feature alone would likely provide significant cost reductions over other chiral agents that can only be used for a limited number of cycles (or time) as they decompose in some fashion. Since a chiral zeolite would be a molecular sieve, it could be used to combine shape-selectivity and selective partitioning from solvents to crystal interiors with the chirality to move man-made catalysts steps closer to the exquisite selectivity of enzymes. Also, chiral molecular sieves would open new types of chiral catalysis, as they could be used at much higher temperatures and pressures than enzymes in liquid-phase reactions, and be exploited to catalyze vapor-phase reactions (both in flow reactors if needed). Thus, it is obvious that there are a lot of new reaction pathways that could be explored if chiral molecular sieves could be synthesized.

The idea of preparing a chiral zeolite gained importance when Newsam et al.[4] and Higgins et al.[5] published the structure of zeolite beta (*BEA – molecular sieve framework types are designated by three-letter codes that define their three-dimensional connectivity of oxide tetrahedra[6]). They showed that zeolite beta (Figure 1) is an intergrowth of two polymorphs (A and B), and that polymorph A contains a three-dimensional pore system where the pores along the c-direction of the crystal follow a four-fold screw axis to define a helix (right- or left-handed:

$P4_122$ or $P4_322$, respectively).[4,5] Newsam and co-workers also recognized the consequences of the helical pore system as having the potential to enable zeolite beta to be a chiral catalyst.[4] While there are a number of zeolites and molecular sieves that are inherently chiral, e.g., *BEA, CZP, GOO, -ITV, JRY, LTJ, OSO, SFS, STW,[6] all these powdered, polycrystalline samples are racemic.

We began work on synthesizing a chiral zeolite in 1987, and it was not until 2017 that we reported the first successful preparation of an enantiomerically enriched, polycrystalline molecular sieve.[7] Here, I present how we began our work in 1987, and the various ups and downs of a thirty-year journey to success. I report various steps in our understanding towards our ultimate objective that are available in the open literature, and also provide insights to our thinking that have not been recorded previously. My hope is to provide an interesting story on how a scientific objective of importance was achieved.

Initiating the Goal of Synthesizing a Chiral Zeolite in the 1980s

In the early 1980's, my research program in Chemical Engineering at Virginia Tech focused on synthesizing organometallic complexes within the pores of zeolites to create solid catalysts for propylene hydroformylation. Our initial system involved rhodium containing zeolites. Along with my collaborator, Professor Brian Hanson (Chemistry, Virginia Tech), we developed synthetic methods to make rhodium carbonyl and carbonyl phosphine complexes in zeolites X and Y, and performed both vapor and liquid phase hydroformylation reactions.[8-11] Since the desired products are linear aldehydes/alcohols, we ultimately moved to zeolite A in attempts to take advantage of the small pore zeolite to impart shape-selectivity. With zeolite A, we had to develop methods to synthesize the zeolite around the metal complex.[12-15] When we were in the middle of these studies, Dr. Norman Herron at Dupont published the synthesis of cobalt SALEN complexes in zeolite Y, and coined the term molecular "Ship in a Bottle."[16] For me, Norm did a great service to the community by developing a terminology that made the chemistry more understandable.

At that time, many Virginia Tech faculty had significant working relationships with scientists at Dow Chemical. Through their connections, I was introduced to Dr. Juan Garces at Dow. Juan noted our work on synthesizing zeolites around transition metal complexes, and initiated a research program between our research groups and Dr. Dom Tomalia. The concept was to use Dom's dendrimers as organic structure-directing agent (OSDA) to see if zeolites could be prepared with pores larger than 1 nm. Shortly after that project initiated, I received the Presidential Young Investigator Award from the NSF in 1985 (has morphed into the Career Award). At that time, NSF provided base funding and then matching funds if company support could be obtained. Dow completely funded my award, and this joint program provided a five year research effort where we attacked a number of significant questions in the area of zeolites and molecular sieves: (i) could a molecular sieve with pores comprised of greater than 12 tetrahedral atoms be synthesized?, (ii) could a molecule sieve with a positive framework be prepared?, and (iii) could a shape-selective base catalysts be created using a zeolite? This program led to the discovery of VPI-5, the first molecular sieve with pores comprised of greater

than 12 tetrahedral atoms.[17] Additionally, we proved that a crystalline oxide with only tetrahedral atoms (bridged by oxygens) cannot ever form a positive framework.[1,3] We also made progress on creating solid base catalysts using zeolites by preparing zeolites with clusters of cesium oxide in the pore system.[18,19] That technology led to an interesting base-catalyzed reaction by workers at Merck.[3]

While we were working on addressing these questions in the field of zeolites and molecular sieves, one of the students in my research program, Juan Arhancet, raised the issue of whether or not a chiral zeolite could be synthesized. Juan was interested in chiral catalysis, and his candidacy report involved two ideas for creating asymmetric catalysts: (i) a new immobilized catalyst system that we denoted "supported aqueous phase catalysis" and (ii) enantioselective induction by a molecular sieve.[20] Juan proposed to create a chiral zeolite by the use of a chiral OSDA, even though there was no evidence that this could occur. At Juan's candidacy exam, my colleague Professor David Cox asked (paraphrased) "How many years do you think this will take?" Dave correctly implied that the proposed project appeared to be so speculative that it would likely not be doable within the timeframe of a single PhD thesis project. We now know that Professor Cox was correct in that it took 30 years to succeed! Instead of pursuing the synthesis of a chiral zeolite (at my suggestion - I think that he was not too happy with me!) Juan proceeded to invent "supported aqueous phase catalysis" (SAPC).[21] This new catalyst system ultimately led to interesting chiral catalysis by another student (Kam-to Wan).[22]

While Juan was investigating the SAPC system, workers at Exxon and Mobil published the structure of zeolite beta.[4,5] Dr. Higgins (Mobil) was a graduate of Virginia Tech, and returned to give a lecture on the elucidation of zeolite structures. In that lecture, he presented the structure of zeolite beta (was at about the time of the publications). After Dr. Higgins' lecture, Juan and I discussed going after the synthesis of chiral zeolite beta by targeting an enantiomer of polymorph A. I had the Chem-X software in my lab, and Juan estimated interaction energies between proposed chiral OSDAs and polymoph A. We were not convinced that the energies were of significance, but we used this information to guide our thinking. Unfortunately, none of these molecules were able to act as OSDAs. Subsequently, Juan did prepare an interesting zeolite beta sample that we have described previously.[2,3] We never discussed the organic molecule that was used to prepare this sample because I was concerned about the toxicity of it. Juan methylated strychnine and used it as the OSDA. The interesting zeolite beta sample he obtained did contain organic in the as-synthesized form, but it was not the intact methylated strychnine. At that time, we were not able to exactly determine the nature of the remaining organic. The powder X-ray diffraction pattern of the sample is reproduced in Figure 2. While numerous reports have described attempts to ascertain the amounts of polymorphs A and B in zeolite beta by simulating the lowest d-spacing diffraction lines, what is more important to the pattern shown in Figure 2 is the peak at around 10 degrees 2-theta. In order to have that reflection, the sample must contain blocks of polymorph A of significant size.[4] However, the question that remained was whether or not these blocks of polymorph A contained enantioenrichment. In an attempt to address this question, we performed enantioselective adsorption and catalysis. The sample was used to ring-open trans-

stilbene (see Figure 2), and gave an ee of ca. 5% (R,R-diol) while "normal" zeolite beta was zero. Additionally, a racemic mixture of the diols showed a small preferential adsorption of the R,R diol and "normal" zeolite beta did not. There are many issues with these results. The choice of trans-stilbene was not arbitrary, as we attempted to match the size of the molecule to the dimension of the helical pore in polymorph A. This is a critical point that will be discussed below.

This first attempt to prepare a chiral molecule sieve stimulated our thinking, and raised a number of points that I felt that we needed to address before we would have a realistic chance of not only preparing a chiral molecular sieve, but also convincing ourselves and others that we had truly accomplished this feat. Some of the most important issues were:

1. Can further understandings of zeolite assembly and OSDA design be obtained in order to have a chiral OSDA lead to the synthesis of a chiral molecule sieve?
2. How can one prove that a powdered sample (with crystals too small for single crystal X-ray analysis) have chirality?
3. How can chiral function (catalysis, adsorption, etc.) be proven when the chirality is measured over a long distance (not point chirality like with a molecule)?
4. What are the proper controls that can be designed to give confidence in the results whether they are structural or functional?

Below, I will discuss how we addressed these questions, as each was critical to our successful synthesis and characterization of the first enantioenriched polycrystalline molecular sieve.

Juan Arhancet is the person who I give credit for initiating our work in synthesizing a chiral molecule sieve. While he was not able to meet the ultimate objective, his early work set the stage for what was to come. Juan invented SAPC during his PhD work, and then went on to have a very successful career at Shell and Monsanto. At a later time, Kam-to Wan departed Caltech to work at Monsanto. Interestingly, the two people who independently invented and then successfully made SAPC perform asymmetric catalysis worked together at Monsanto!

The Transition to Caltech and Concentrated Efforts on Chirality in the 1990-2000s

In 1990-1991, I moved from Virginia Tech to Caltech. Now at Caltech, I immediately focused on question 1 (*vide supra*). When I first reported the structure of VPI-5 at a meeting in Belgium (1987), I was introduced to Dr. Stacey Zones of Chevron. Stacey is a world leader in the use of OSDAs for zeolite and molecular sieve synthesis. My move to the west coast greatly assisted our initiation of a long-term friendship and collaboration. As we began our collaborative investigations, I tasked Sandra Burkett (Chemistry PhD student) to begin to work on understanding better the molecular-level interactions between OSDAs and the inorganic components, and Raul Lobo (Chemical Engineering PhD student) to begin to focus investigations on how to prepare a chiral molecular sieve. These studies provided insights into the mechanisms of OSDA structure direction.[23-26]

In 1992, Raul and I published a review on zeolite and molecular sieve synthesis where we summarized the field that included syntheses that employed OSDAs.[2] We used this review to also bring out our current thinking on what would be needed to synthesize a chiral zeolite. We first discussed zeolite beta, and then commented on how one would have to have a synthetic methodology that would make polymorph A and then also an enantiomer of polymorph A. We suggested that it would be a more straightforward pathway to a chiral zeolite if each crystal was not an intergrowth (each crystal of quartz is a single enantiomer), and Raul created a hypothetical structure (based on the building units, would likely to be high-silica and thus amenable to structure direction) to illustrate the point (Figure 6 of ref. 2). Additionally, and most importantly, we clearly discussed the issues of preparing and using a chiral OSDA. First, we cannot envision the synthesis of a chiral zeolite without the use of a chiral OSDA since the two enantiomorphs of the structure would have the same energy. That is to say, the chiral OSDA is necessary to energetically distinguish between the two enantiomorphs by separating the energies of the OSDA-framework composites through chiral OSDA-chiral framework interactions (one enantiomer of the OSDA will interact differently to the two enantiomers of the framework). This feature was critical to our ultimate success (*vide infra*). Second, we enumerated attributes of the OSDAs that we believed would be necessary for success. Some of these are:[2]

1. OSDA must be chiral.
2. OSDA must be of sufficient size to interact with the framework over distances that determine the chirality of the framework, e.g., a length that can distinguish the direction of a helical turn in the pore.
3. OSDA must be stable to the synthesis conditions.
4. OSDA must be rigid to minimize obtainable confirmations during the synthesis.
5. OSDA must not be able to rotate with the pore structure or the chirality will be lost.

These criteria were useful for guiding our investigations. In addition to continuing our fundamental studies on OSDA design and how structure direction occurs,[27] we began synthetic efforts with chiral OSDAs. We felt that (-)sparteine would be an interesting chiral organic to convert into a chiral OSDA. Raul methylated it to create N(16) methylsparteinium, and used that charged molecule as an OSDA to prepare SSZ-24.[28] While N(16) methylsparteinium did not lead to a chiral framework, it did provide for the synthesis of CIT-5.[29,30] This type of OSDA satisfied a number of the attributes that we sought in an OSDA, but as Raul showed by variable temperature NMR (290-370K), the molecule could rotate in the pores of SSZ-24.[31] Thus, attribute 5 was not achieved with this system.

During the 1990's and early 2000's, we continued our efforts to understand structure direction with OSDAs and explored a number of chiral ones.[27,32,33] I summarized our efforts in 2003 with a paper I titled "Reflections on routes to enantioselective solid catalysts."[33] In Table 2 of that publication (ref. 33), I listed the various chiral OSDAs we synthesized and tested. Overall, none of these molecules had all 5 attributes listed above. Thus, one way to describe our efforts over this time period is a comment made by Master Yoda to Luke Skywalker in Star Wars the

Last Jedi "the greatest teacher, failure is." While we failed to synthesize a chiral molecular sieve, our understandings of what would be necessary to do so continued to improve.

On the route to successfully synthesizing a chiral molecular sieve – the 2010's

In the first half of this decade, I had two meetings that ultimately provided key components to our creation of the first chiral molecular sieve. First, over a dinner in Houston in 2012, I discussed with Professor Michael Deem the problems associated with using chiral OSDAs to prepare chiral frameworks. At that time, Michael described how he could computationally predict chemically synthesizable OSDAs.[34] While there have been a number of reports on computational investigations of OSDA-framework interactions and how they could lead to new structures, I was still not convinced of that strategy. However, Michael's enthusiasm for using his methodology was infectious, and I agreed to test it out on a problem with my research group. If the initial test worked, then we planned to move into its use for chirality. Success with chirality would be a real "feather in his cap" for this methodology. Below, I will describe how we began this collaboration. Second, over dinner (is there a trend here?) at the Dallas ACS meeting in the Spring of 2015, I had a discussion with Professor Osamu Terasaki about how one might be able to ascertain chirality of a powdered sample with crystals too small for single-crystal, X-ray diffraction. We talked about various microscopy methods and their feasibilities. As described below, these meetings brought two critically important concepts to our program that was increasing in the number of collaborators. These interactions ultimately provided two significant parts to the successful synthesis and characterization of the first enantiomerically enriched, polycrystalline molecular sieve.[7]

In 2008, Tang et al. reported the germanosilicate STW.[35] Subsequently, in 2012, Rojas and Camblor showed that STW could be prepared as a pure-silica framework (pure-silica materials have much better thermal and hydrothermal stabilities).[36] From these publications, we recognized that STW could be a target framework of the type that we had been seeking for some time. Recall how Raul created a hypothetical structure to illustrate the point of having crystals that were only single enantiomers (*vide supra*).[2] STW had the potential to satisfy that criterion (subsequently shown to be true, *vide infra*). Based on the work of Rojas and Camblor, we selected the pure-silica synthesis of STW to test the computational procedures of Professor Deem. In that study, we learned how to combine our "chemical intuition and understandings of OSDA properties and behaviors" with Professor Deem's computational methods to successfully find OSDAs that crystallize pure-silica STW.[37] Of importance, we found that computational energies of two molecules could be the same but one out performed the other in terms of ease of STW synthesis. We speculated that this difference was due to the fact that the lesser performing OSDA contained an ethyl group that could rotate and thus have multiple conformations. If this is the case (we could not prove this point), then the results would be consistent with our previous findings about minimizing conformations of the OSDAs during

synthesis. This highly successful synthesis study convinced us to now proceed to chirality with OSDAs and STW.

Successfully synthesizing the first enantiomerically enriched, polycrystalline molecular sieve[7]

After all the years of study, we were finally in a good position to take advantage of advances in our understanding of structure direction and methods for characterizing powdered samples. To begin, we first had to develop a strategy that would create materials that would provide all the proper controls for structure and function determinations. Figure 3 illustrates our strategy. That is, we must be able to prepare OSDAs that are pure enantiomers (both) in order to synthesize the two enantiomers of STW. The set of STW materials for study with proper controls would be: (i) S-STW (from S-OSDA), (ii) R-STW (from R-OSDA), (iii) racemic STW from physically mixing a one-to-one ratio of S-STW and R-STW and (iv) racemic STW from racemic OSDA (S-STW should show equal and oppose ee to R-STW, and the racemic samples an ee of zero). Second, we had to design a chiral OSDA for STW. Based on our previous work with Professor Deem that employed imidazole OSDAs for racemic STW,[37] and knowing that we needed an OSDA with attributes 1-5, we worked with Professor Deem to design dimers of imidazoles. Table 1 illustrates some of our results and includes the OSDA we selected. Of importance, we were always mindful of how difficult the organic synthesis would be. That point helped select which molecule we prepared. The OSDA used had all the right attributes, and showed very large energy differences between the two enantiomorphs of STW (Table 1). While the synthesis of pure enantiomers of this OSDA was not trivial, it was doable. [7]

Successful synthesis of germanosilicate STW using pure enantiomers of the OSDA was achieved. Now the issue was to show through both structural and functional characterization that there was some enantioenrichment. Clearly, the X-ray pattern defined the STW topology, and circular dichroism revealed that the OSDA within the pores of the STW remained chiral.[7] Since the time of my meeting with Professor Terasaki, he and his co-workers had developed a methodology to determine the handedness of crystals using high resolution transmission electron microscopy.[38] Ma et al. showed that individual crystals of STW were in fact single enantiomorphs like we expected (hoped!). Using this methodology, six crystals of S-STW, R-STW and racemic STW were analyzed. For both S-STW and R-STW, 5 of the 6 crystals revealed the correct enantiomorph (that expected from the enantiomer of the OSDA used), while the racemic sample did show 3 crystals of each handedness. Possible reasons for not complete purity in S-STW and R-STW are: (i) racemic seed crystals were employed in the synthesis and maybe one of the crystals analyzed was a seed crystal, (ii) there could be some OSDA degradation (although we could not find bulk evidence for this) leading to non-chiral organics, and (iii) the inherent nature of the crystallization process may not lead to 100% ee.[7]

To prove chiral function, we performed both adsorption and catalysis experiments.[7] Here, I will discuss the catalysis (refer to Table 2). We selected the epoxide ring-opening reaction for study. First, note that the magnitude of the ee for the R-STW is similar to the S-STW but in the opposite direction, and that the ee for the racemic STW is zero. Having this set of

solids provided for the types of control experiments that lead to convincing conclusions. Second, the ee's increase with the length of the epoxide. This makes good sense since the chirality in STW is over a long length scale. In Figure 4, the sizes of the epoxides investigated are schematically illustrated next to the OSDA used and the helical pore of STW. Since the size of the OSDA is sufficient to dictate the chirality of STW, one may speculate that as that size is approached then chiral induction may occur with the reaction. Note that this trend is observed (Table 2). However, it is just not only the length of that single dimension that matters, but also the size of the alcohol that is used for ring-opening (ee's increase with increasing size of the R group in the alcohol (ROH)). One caution though, as the ee's increase in this system, the conversion decreases. These initial results clearly show that chiral catalysis can be achieved with a chiral molecular sieve. This area of study is ideal for computer simulation. I have no doubt that other reactions and better ee's can be obtained using chiral molecular sieve catalysts.

Future

Now that the first enantiomerically enriched, polycrystalline molecular sieve has been prepared and shown to function for chiral adsorption and catalysis,[7] there is much work ahead. As far as applications are concerned, chiral separation and catalytic processes are obvious directions for investigation. Chiral, germanosilicate STW has issues that need to be solved prior to application. For example, these materials are not very stable, and the use of Ge and F (both required in the synthesis that has been reported[7]) would likely be prohibitive for large-scale syntheses. If chiral, high-silica STW could be prepared, this would be significant. We note that the OSDAs that gave good results in preparing high-silica STW had calculated stabilization energies superior[37] to that of the chiral OSDA that produced the chiral, germanosilicate STW.[7] Work continues on designing OSDAs for chiral STW,[39,40] and the synthesis of chiral, high-silica STW should be achievable. Additionally, there are a multitude of fundamental issues that require investigation. Of particular importance would be to understand the relationships between the long-range chirality in these types of systems and the induction of chirality that can occur in adsorption and catalysis. Studies of this nature for adsorption are already apprearing.[41]

Acknowledgements

I hope that this brief expose of how my research program went from initial concept to successful discovery provides some insights to how research can proceed. In today's world where step-by-step proposed experiments with many yearly milestones are becoming more the norm for receiving support to conduct research, it is clear to me that this is not how breakthrough research occurs. One must have the freedom to have time to explore, to think, to learn and to have lots of failures. And, one needs a bit of luck (take it when you can get it!). I am fortunate that we had all those attributes over many years, and that we were able to take advantage of them to ultimately achieve our objective.

I thank the many students and co-workers that I have had the pleasure of working with over the years (whose names appears on our publications). I also thank the various sources of funding such as NSF, DOE, Dow and Chevron for supporting our efforts. As I tell the members of my research group, what is nice about being in academia, you can work on problems you would like to work on IF you can find someone else to pay for them! I would especially like to thank Dr. Stacey Zones and Chevron for providing us tremendous freedom to explore and understand zeolite and molecular sieve synthesis. Special thanks go to Chevron for supporting our work on creating a chiral molecular sieve. It is worthy of noting a company that would have no direct use for a chiral molecular sieve was encouraging of our studies as they realized that information needed to create such a material could be useful to their programs on synthesizing molecular sieve for other uses.

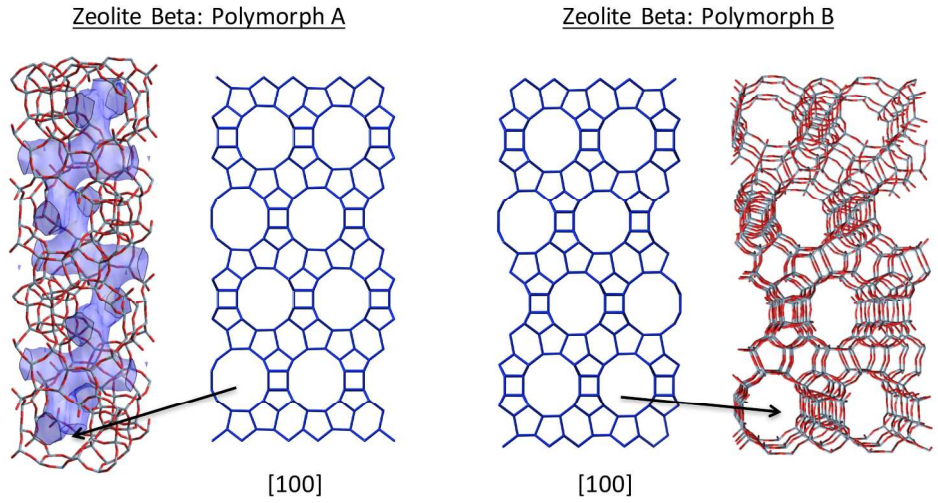


Figure 1: Schematic representations of the zeolite beta structure. Zeolite beta is an intergrowth between two polymorphs. The [100] projections show the arrangements of the 12 tetrahedral atoms that make up the large pores (line segments represent bridging oxygen atoms and their intersections are where the tetrahedral atoms reside (strictly aluminum and silicon to be called a zeolites, but can be other atoms such as phosphorus, germanium, etc. when denoted as a molecular sieve). Polymorph A has a helical pore (and as such has two enantiomers: left and right handed screw axis), while polymorph B does not. Figure created by Jong Hun Kang (Caltech).

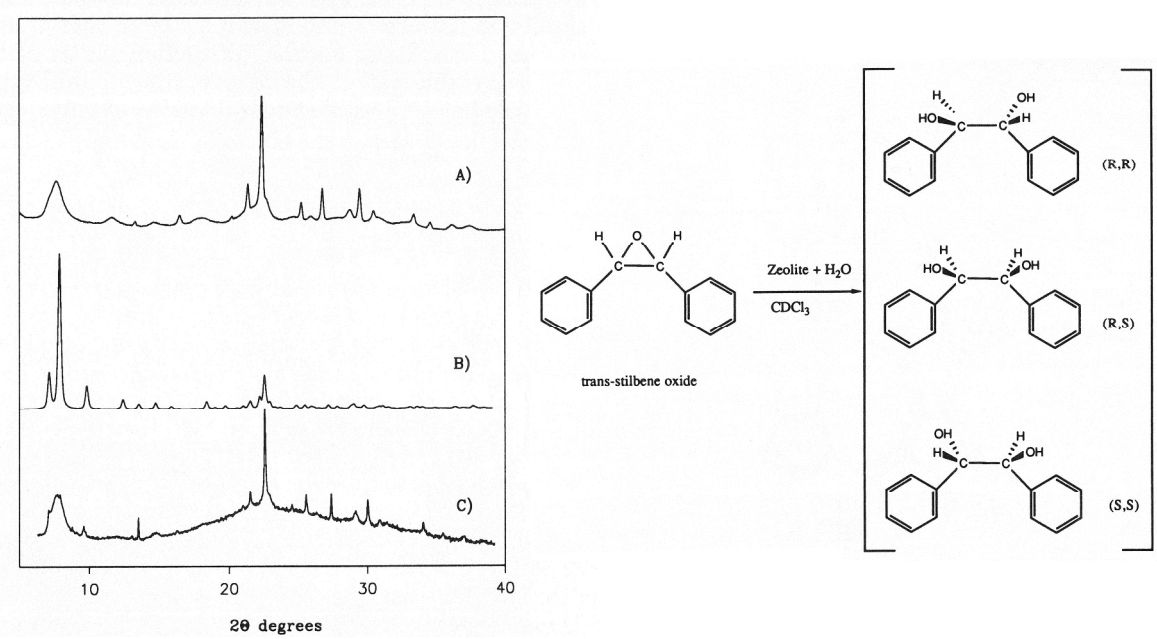


Figure 2. Left: X-ray powder diffraction pattern of (A) as-synthesized zeolite beta, (B) pure (no organic present polymorph A (simulated), and (C) zeolite beta synthesized in the presence of a chiral organic molecule. Right: Reactions on zeolite beta. Adapted with permission from Davis, M. E.; Lobo, R. F. *Chem. Mater.* 1992, 4, 756-768. Copyright (1992) American Chemical Society,

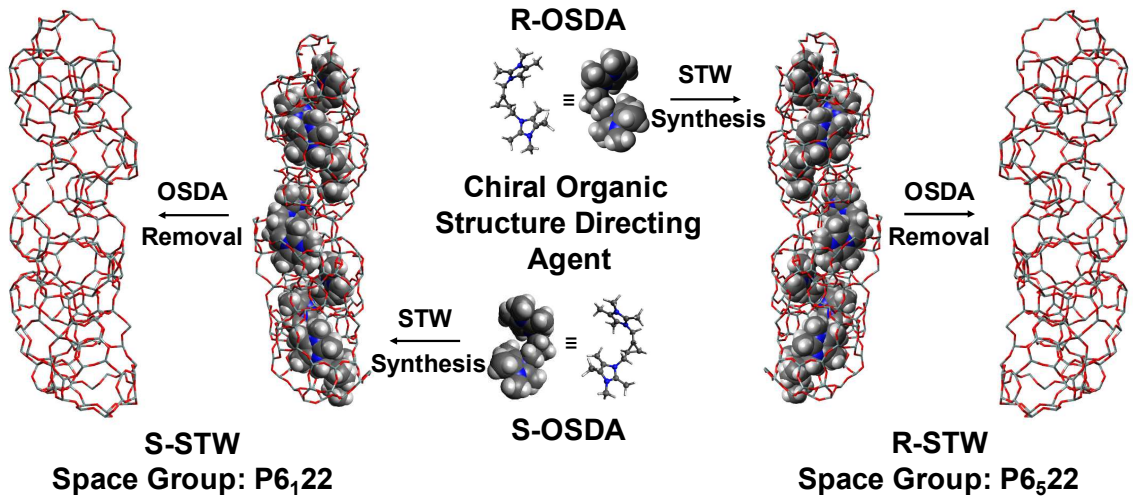


Figure 3. Strategy for synthesizing chiral STW with proper controls as described in the text. Reproduced from Brand, S. K.; Schmidt, J. E.; Deem, M. W.; Daeyaert, F.; Ma, Y; Terasaki, O.; Orazov, M; Davis, M. E. *Proc. Natl. Acad. Sci. USA* 2017, 114, 5101-5106.

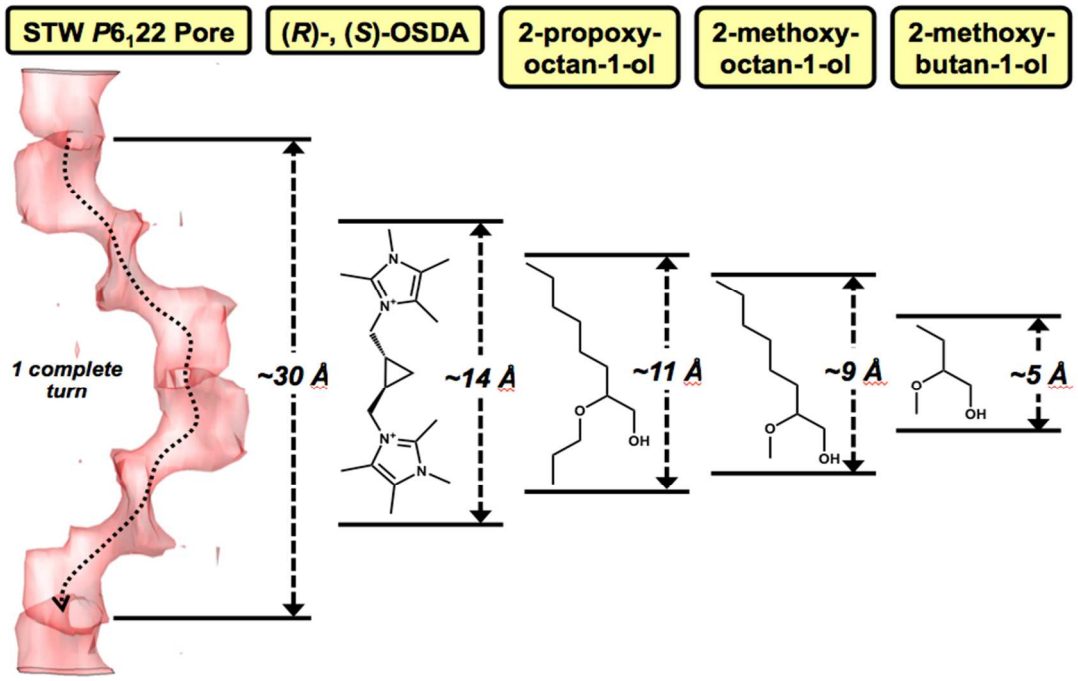


Figure 4. Schematic illustration of the helical pore of STW, the OSDA agent used in its synthesis, and epoxides reacted.

Table 1. Possible chiral OSDAs. The one in the box is the OSDA that was prepared. From ref. 7.

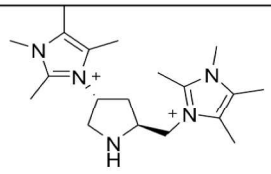
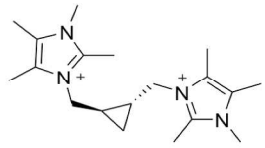
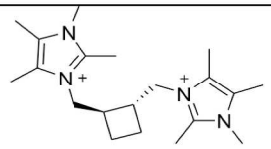
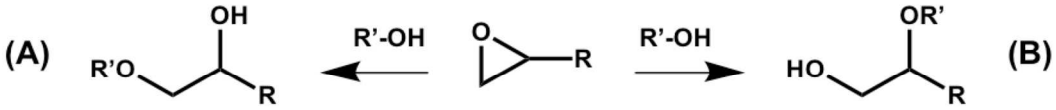
Proposed SDA	$E_{enantiomer\ 1}$ (i.e. $P6_122$) kJ/mol-Si	$E_{enantiomer\ 2}$ (i.e. $P6_522$) kJ/mol-Si
	-16.32	-14.60
	-15.27	-1.58
	-14.65	-1.37

Table 2. Summary of reaction results. Data listed with superscript b are from ref. 7.



Enantiomeric excesses (ee's, %) from 1,2-epoxyalkane ring-opening over Al-containing racemic, (*R*)-, and (*S*)-STW catalysts [a]

Substrate (R)	Nucleophile (R')	(*R*)-STW		Racemic STW		(*S*)-STW	
		A / %	B / %	A / %	B / %	A / %	B / %
1,2-epoxybutane	Methanol [b]	-0.1	2.3	0.1	0.1	0.0	-2.3
1,2-epoxyhexane	Methanol [b]	1.3	2.8	0.2	-0.9	-2.0	-3.5
1,2-epoxyoctane	Methanol [b]	4.1	9.9	1.1	-0.9	-4.4	-10.7
	Ethanol	4.2	9.3				
	1-propanol	3.8	22.5				
	1-butanol	2.0	22.9				

[a] Reaction conditions: 20 mmol substrate, 5 g nucleophile, 20 mg catalyst, T = 50 °C, t = 48 h

References:

1. Davis, M. E. Zeolites and Molecular Sieves: Not Just Ordinary Catalysts. *Ind. Eng. Chem. Res*. 1991, 30, 1675-1683.
2. Davis, M. E.; Lobo, R. F. Zeolite and Molecular Sieve Synthesis. *Chem. Mater.* 1992, 4, 756-768.
3. Davis, M. E. New Vistas in Zeolite and Molecular Sieve Synthesis. *Acc. Chem. Res.* 1993, 26, 111-115.
4. Newsam, J. M.; Treacy, M. M. J.; Koetsier, W. T.; de Gryter, C. B. Structural Characterization of Zeolite-Beta. *Proc. R. Soc. London A* 1988, 420, 375-405.
5. Higgins, J. B.; LaPierre, R. B.; Schlenker, J. L.; Rohrman, A. C.; Wood, J. D.; Kerr, G. T.; Rohrbaugh, W. J. The Framework Topology of Zeolite-Beta. *Zeolites* 1988, 6, 445-538.
6. IZA (2017) IZA Structure Commission. Available at www.iza=structure.org
7. Brand, S. K.; Schmidt, J. E.; Deem, M. W.; Daeyaert, F.; Ma, Y; Terasaki, O.; Orazov, M; Davis, M. E. Enantiomerically Enriched, Polycrystalline Molecular Sieves. *Proc. Natl. Acad. Sci. USA* 2017, 114, 5101-5106.
8. Hanson, B. E.; Davis, M. E.; Taylor, D.; Rode, E. Intrazeolite Rhodium Carbonyl and Rhodium Carbonyl Phosphine Complexes. *Inorg. Chem.* 1984, 23, 52-56.
9. Rode, E.; Davis, M. E.; Hanson, B. E. Rhodium Zeolites as Bifunctional Catalysts for the Synthesis of 2-Methyl-3-Hexanone and 4-Heptanone from Propylene, CO, and H_2. *J.C.S. Chem. Commun.* 1985, 1477-1478.
10. Davis, M. E.; Butler, P. M.; Rossin, J. A.; Hanson, B. E. Hydroformylation of 1-Hexene by Soluble and Zeolite Supported Rhodium Species. *J. Mol. Catal.* 1985, 31, 385-395.
11. Rode, E. J.; Davis, M. E.; Hanson, B. E. Propylene Hydroformylation on Rhodium on Rhodium Zeolites X and Y. *J. Catal.* 1985, 96, 563-573.
12. Rossin, J. A.; Davis, M. E. Synthesis of Rhodium Containing Zeolite A. *J.C.S. Chem. Commun.* 1986, 234-236.
13. Davis, R. J.; Rossin, J. A.; Davis, M. E. Hydroformylation by Rhodium Zeolite A Catalysts. *J. Catal.* 1986, 98, 477-486.
14. Davis, M. E.; Saldarriaga, C.; Rossin, J. A. Synthesis and Catalysis of Transition Metal Containing Zeolite A. *J. Catal.* 1987, 103, 520-523.
15. Wu, J. C. S.; Goodwin, J. G., Jr.; Davis, M. E. Catalytic Properties of Ru/A Zeolite Catalysts Prepared by the Synthesis Method. *J. Catal.* 1990, 125, 488-500.
16. Herron, N. A Cobalt Oxygen Carrier in Zeolite Y – A Molecular Ship in a Bottle. *Inorg. Chem.* 1986, 25, 4714-4717.
17. Davis, M. E.; Saldarriaga, C.; Montes, C.; Garces, J.; Crowder, C. A Molecular Sieve with Eighteen-Membered Rings. *Nature* 1988, 331, 698-699.
18. Hathaway, P. E.; Davis, M. E. Base Catalysis by Alkali Modified Zeolites. I. Catalytic Activity. *J. Catal.* 1989, 116, 263-278.
19. Hathaway, P. E.; Davis, M. E. Base Catalysis by Alkali Modified Zeolites. II. Nature of the Active Site. *J. Catal.* 1989, 116, 279-284.
20. Arhancet, J. P. Candidacy Report, Chemical Engineering, Virginia Tech, 1987.
21. Arhancet, J. P.; Davis, M. E.; Merola, J. S.; Hanson, B. E. Hydroformylation by Supported Aqueous Phase Catalysis. *Nature* 1989, 339, 454-455.

22. Wan, K. T.; Davis, M. E. The Design and Synthesis of a Heterogeneous Asymmetric Catalyst. *Nature* 1994, 370, 449-450.
23. Burkett, S. L.; Davis, M. E. Mechanism of Structure Direction in the Synthesis of Si-ZSM-5: An Investigation by Intermolecular ^{1}H-^{29}Si CP/MAS NMR. *J. Phys. Chem*. 1994, 98, 4647-4653.
24. Burkett, S. L.; Davis, M. E. Mechanisms of Structure-Direction in Pure-Silica Zeolite Synthesis. I. TPA-ZSM-5. *Chem. Mater.* 1995, 7, 920-928.
25. Burkett, S. L.; Davis, M. E. Mechanism of Structure-Direction in Pure-Silica Zeolite Synthesis. II. Hydrophobic Hydration and the Origin of Structure Specificity. *Chem. Mater.* 1995, 7, 1453-1463.
26. Lobo, R. F., Zones, S. I.; Davis, M. E. Structure-Directing in Zeolite Synthesis. *J. Inclus. Phenom. Mol. Rec. Chem.* 1995, 21, 47-78.
27. Kubota, Y.; Helmkamp, M. M.; Zones, S. I.; Davis, M. E. Properties of Organic Cations that Lead to the Structure-Direction of High-Silica Molecular Sieves. *Microporous Mater*. 1996, 6, 213-229.
28. Lobo, R. F.; Davis, M. E. Synthesis and Characterization of Pure-Silica and Boron Substituted SSZ-24 Using N(16) Methylsparteinium Bromide as Structure-Directing Agent. *Microporous Mater.* 1994, 3, 61-69.
29. Wagner, P.; Yoshikawa, M.; Lovallo, M.; Tsuji, K.; Tsapatsis, M.; Davis, M. E. CIT-5: A High-Silica Zeolite with 14-Ring Pores. *Chem. Commun.* 1997, 2179-2180.
30. Tsuji, K. Wagner, P.; Davis, M. E. High-Silica Molecular Sieve Synthesis Using the Sparteine Related Compounds as Structure-Directing Agents. *Micropor. Mesopor. Mat*. 1999, 28, 461-469.
31. Lobo, R. F. PhD Thesis, California Institute of Technology, 1994.
32. Lobo, R. F.; Davis, M. E. CIT-1: A New Molecular Sieve with Intersecting Pores Bounded by 10- and 12-Rings. *J. Am. Chem. Soc.* 1995, 117, 3766-3779.
33. Davis, M. E. Reflections on Routes to Enantioselective Solid Catalysts. *Top. Catal.* 2003, 25, 3-7.
34. Pophale, R.; Daeyaert, F.; Deem, M. W. Computational Prediction of Chemically Synthesizable Organic Structure Directing Agents for Zeolites. *J. Mater. Chem. A* 2013, 1, 6750-6760.
35. Tang, L.; Shi, L.; Bonneau, C.; Sun, J.; Yue, H.; Ojuva, A.; Lee, B. L.; Kritikos, M.; Bell, R. G.; Bacsik, Z.; Mink, J.; Zou, X. A Zeolite Family with Chiral and Achiral Structures Built from the Same Building Layer. *Nat. Mater*. 2008, 7, 381-385.
36. Rojas, A.; Camblor, M. A. A Pure Silica Chiral Polymorph with Helical Pores. *Angew. Chem. Int. Ed*. 2012, 51, 3854-3856.
37. Schmidt, J. E.; Deem, M. W.; Davis, M. E. Synthesis of a Specified, Silica Molecular Sieve Using Computationally Predicted Organic Structure Directing Agents. *Angew. Chem. Int. Ed.* 2014, 53, 8372-8374.
38. Ma, Y.; Oleynikov, P.; Terasaki, O. Electron Crystallography for Determining the Handedness of a Chiral Zeolite Nanocrystal. *Nat. Mater*. 2017, 16, 755-759.
39. Lu, P.; Gomez-Hortiguela, L.; Xu, L.; Camblor, M. A. Synthesis of ZTW Zeolites Using Imidazolium-based Dications of Varying Length. *J. Mater. Chem. A* 2018, 6, 1485-1495.

40. Daeyaert, F.; Deem, M. W. In Silico Design of Chiral Dimers to Direct the Synthesis of a Chiral Zeolite. *Mol. Phys.* 2018, DOI: 10.1080/00268976.2018.1492747
41. Bueno-Perez, R.; Balestra, S. R.; Camblor, M. A.; Min, J. G.; Hong, S. B.; Merkling, P. J.; Calero, S. Influence of Flexibility on the Separation of Chiral Isomers in STW-type Zeolite. *Chem. Eur. J.* 2018, 24, 4121-4132.

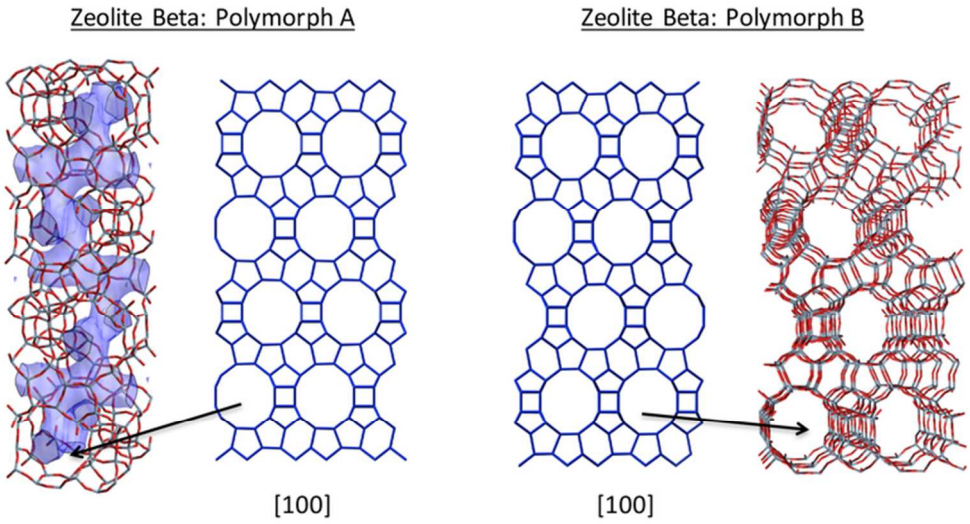


Figure 1

67x35mm (300 x 300 DPI)

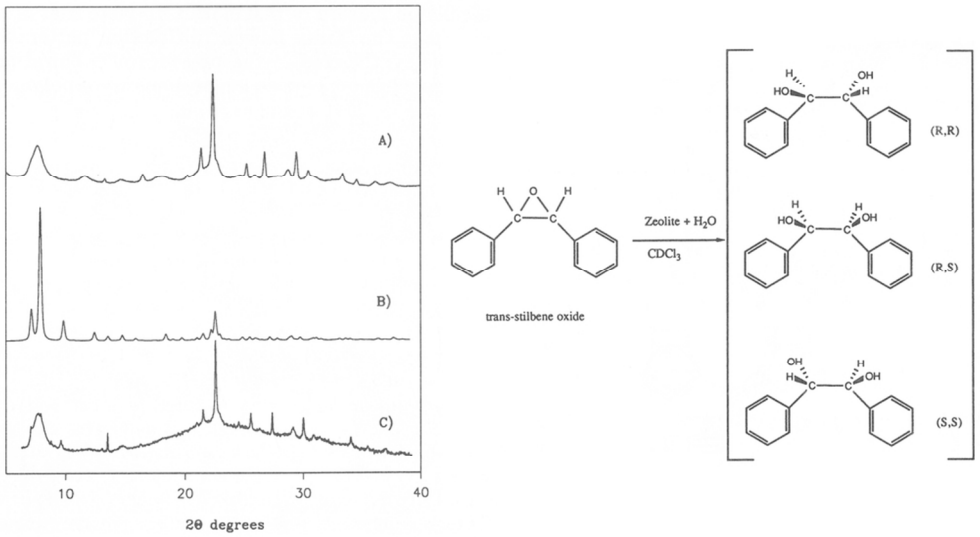


Figure 2

86x48mm (300 x 300 DPI)

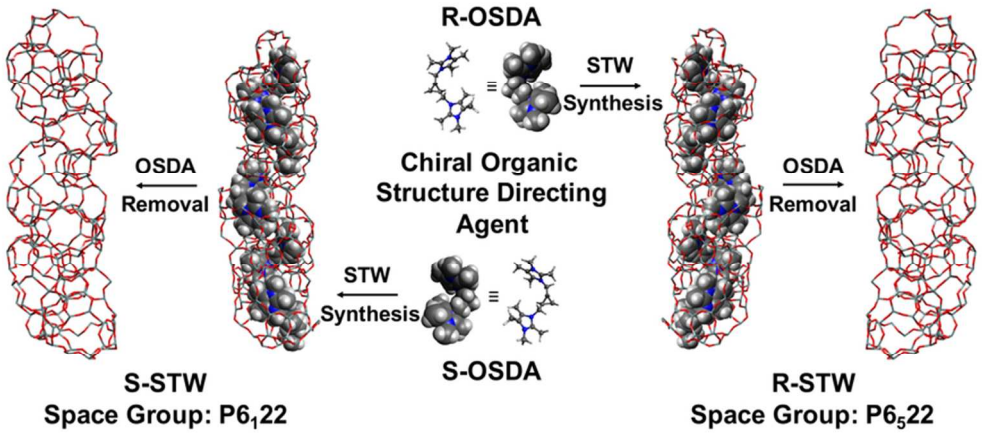
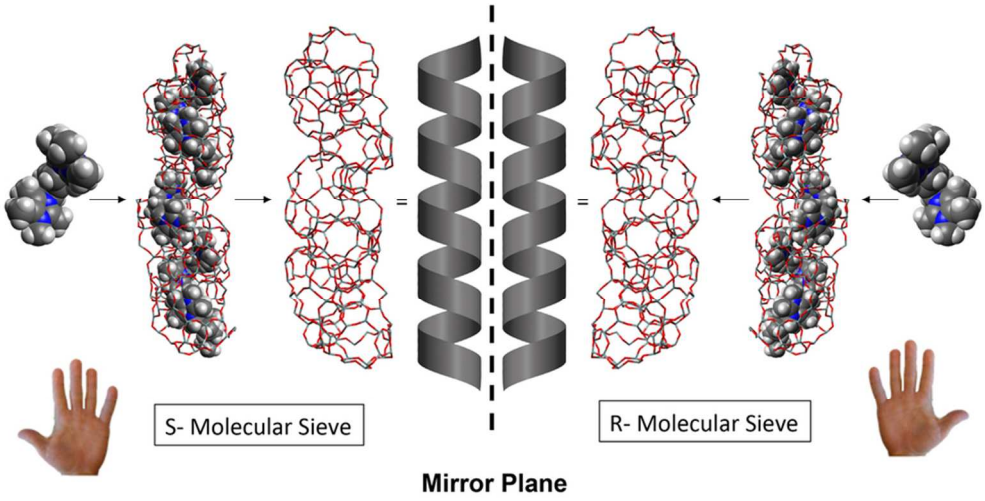


Figure 3

74x33mm (300 x 300 DPI)



TOC graphic

41x20mm (600 x 600 DPI)